SEQUENCE LISTING

<110> Micromet AG <120> Compositions comprising polypeptides <130> MIC-017 PCT <150> EP 03 027 511.9 <151> 2003-11-28 <160> 6 <170> PatentIn version 3.1 <210> 1 <211> 504 <212> PRT <213> artificial sequence <220> <223> Construct 1: VL(CD19)-VH(CD19)-VH(CD3)-VL(CD3) <400> 1 Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly 10 Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp 25 Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met 150 Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln 195 200

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg 210 215 220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp 225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp 245 250 255

Ile Lys Leu Gln Gln Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser 260 265 270 .

Val Lys Met Ser Cys Lys Thr Ser Gly Tyr Thr Phe Thr Arg Tyr Thr 275 280 285

Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly 290 295 300

Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys 305 310 315 320

Asp Lys Ala Thr Leu Thr Thr Asp Lys Ser Ser Ser Thr Ala Tyr Met 325 330 335

Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys Ala 340 345 350

Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr 355 360 365

Thr Leu Thr Val Ser Ser Val Glu Gly Gly Ser Gly Gly Ser Gly Gly 370 375 380

Ser Gly Gly Ser Gly Gly Val Asp Asp Ile Gln Leu Thr Gln Ser Pro 385 390 395 400

Ala Ile Met Ser Ala Ser Pro Gly Glu Lys Val Thr Met Thr Cys Arg
405 410 415

Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Ser Gly
420 425 430

Thr Ser Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly
435 440 445

Val Pro Tyr Arg Phe Ser Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu 450 455 460

Thr Ile Ser Ser Met Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln 465 470 475 480

Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu 485 490 495

Leu Lys His His His His His 500

<210> 2

<211> 505

<212> PRT

<213> artificial sequence

<220> <223> Construct 2: VH(CD19)-VL(CD19)-VH(CD3)-VL(CD3) <400> 2 Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Ala Met Asp 105 Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly 120 Ser Gly Gly Gly Ser Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile 150 Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr 185 Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser 200 Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr 230 Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Ser Asp Ile Lys Leu Gln Gln Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala 265 Ser Val Lys Met Ser Cys Lys Thr Ser Gly Tyr Thr Phe Thr Arg Tyr 275 Thr Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile 295 Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe

315 310 305

Lys Asp Lys Ala Thr Leu Thr Thr Asp Lys Ser Ser Ser Thr Ala Tyr 330 325

Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly

Thr Thr Leu Thr Val Ser Ser Val Glu Gly Gly Ser Gly Gly Ser Gly

Gly Ser Gly Gly Ser Gly Gly Val Asp Asp Ile Gln Leu Thr Gln Ser 395

Pro Ala Ile Met Ser Ala Ser Pro Gly Glu Lys Val Thr Met Thr Cys 410

Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Ser

Gly Thr Ser Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser

Gly Val Pro Tyr Arg Phe Ser Gly Ser Gly Ser Gly Thr Ser Tyr Ser

Leu Thr Ile Ser Ser Met Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys 470

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu

Glu Leu Lys His His His His His 500

<210> 3

<211> 504 <212> PRT <213> artificial sequence

<223> Construct 6: VH(CD3)-VL(CD3)-VH(CD19)-VL(CD19)

<400> 3

Asp Ile Lys Leu Gln Gln Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala

Ser Val Lys Met Ser Cys Lys Thr Ser Gly Tyr Thr Phe Thr Arg Tyr

Thr Met His Trp Val Lys Glm Arg Pro Gly Gln Gly Leu Glu Trp Ile

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe

Lys Asp Lys Ala Thr Leu Thr Thr Asp Lys Ser Ser Ser Thr Ala Tyr 70

Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly 105 Thr Thr Leu Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly 120 Ser Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Ser Gly Thr Ser Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro 185 Tyr Arg Phe Ser Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Ser Met Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys Ser Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly Ala Glu . Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu 310 Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro

420 425 43

Pro Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro 435 440 445

Pro Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile 450 455 460

His Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser 465 470 475 480

Thr Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys 485 490 495

Ser Gly His His His His His His 500

<210> 4

<211> 503

<212> PRT

<213> artificial sequence

<220>

<223> Construct 8: VH(CD3)-VL(CD3)-VL(CD19)-VH(CD19)

<400> 4

Asp Ile Lys Leu Gln Gln Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala 1 5 10 15

Ser Val Lys Met Ser Cys Lys Thr Ser Gly Tyr Thr Phe Thr Arg Tyr 20 25 30

Thr Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe 50 55 60

Lys Asp Lys Ala Thr Leu Thr Thr Asp Lys Ser Ser Ser Thr Ala Tyr 65 70 75 80

Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Leu Thr Val Ser Ser Gly Gly Gly Gly Gly Gly Gly 115 120 125

Ser Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ala Ile 130 135 140

Met Ser Ala Ser Pro Gly Glu Lys Val Thr Met Thr Cys Arg Ala Ser 145 150 155 160

Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Ser Gly Thr Ser 165 170 175

Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro

Tyr Arg Phe Ser Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile 195 200 205

Ser Ser Met Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp 210 215 220

Ser Ser Asn Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys 225 230 235 240

Ser Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser 245 250 255

Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser 260 265 270

Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln 275 280 285

Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu 290 295 300

Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp 305 310 315 320

Phe Thr Leu Asn Ile His Pro Val Glu Lys Val Asp Ala Ala Thr Tyr 325 · 330 335

His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly Thr 340 345 350

Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly 355 360 365

Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val 370 375 380

Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala 385 390 395 400

Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly 405 410 415

Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr 420 425 430

Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser 435 440 445

Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala 450 460

Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr 465 470 475 480

Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser 485 490 495

Gly His His His His His His 500

<210> 5

<211> 504

<212> PRT

<213> artificial sequence

<220>

<223> Construct 5: VL(CD3)-VH(CD3)-VH(CD19)-VL(CD19)

<400> 5

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly
1 5 10 15

Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

Asn Trp Tyr Gln Gln Lys Ser Gly Thr Ser Pro Lys Arg Trp Ile Tyr

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Tyr Arg Phe Ser Gly Ser 50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Ser Met Glu Ala Glu 65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr 85 90 95

Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys Gly Gly Gly Ser Gly
100 105 110

Gly Gly Gly Ser Gly Gly Gly Ser Asp Ile Lys Leu Gln Gln Ser 115 120 125

Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Met Ser Cys Lys 130 135 140

Thr Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Lys Gln 145 150 155 160

Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg
165 170 175

Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Lys Ala Thr Leu Thr 180 185 190

Thr Asp Lys Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr 195 200 205

Ser Glu Asp Ser Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His 210 215 220

Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Leu Thr Val Ser Ser 225 · 230 235 240

Ser Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly Ala Glu 245 250 255

Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala Ser Gly
260 265 270

Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg Pro Gly 275 280 285

Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr 290 295 300

Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu 305 310 315 320

Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser Glu Asp 325 330 335

Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val Gly Arg 340 345 350

Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val 355 360 365

Ser Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu 385 390 395 400

Gly Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr 405 410 415

Asp Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro 420 425 430

Pro Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro 435 440 445 ...

Pro Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile 450 455 460

His Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser 465 470 475 480

Thr Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys 485 490 495

Ser Gly His His His His His 500

<210> 6

<211> 503

<212> PRT

<213> artificial sequence

<220>

<223> Construct 7: VL(CD3)-VH(CD3)-VL(CD19)-VH(CD19)

<400> 6

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly
1 5 10 15

Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met 20 25 30

Asn Trp Tyr Gln Gln Lys Ser Gly Thr Ser Pro Lys Arg Trp Ile Tyr 35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Tyr Arg Phe Ser Gly Ser 50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Ser Met Glu Ala Glu 65 70 75 80

Asp A	la.	Ala	Thr	Tyr 85	Tyr	Cys	Gln	Gln	Trp 90	Ser	Ser	Asn	Pro	Le u 95	Thr
Phe G	ly .	Ala	Gly 100	Thr	Lys	Leu	Glu	Leu 105	Lys	Gly	Gly	Gly	Gly 110	Ser	Gly
Gly G		Gly 115	Ser	Gly	Gly	Gly	Gly 120	Ser	Asp	Ile	Lys	Leu 125	Gln	Gln	Ser
Gly A		Glu	Leu	Ala	Arg	Pro 135	Gly	Ala	Ser	Val	Lys 140	Met ·.	Ser	Cys	Lys
Thr S 145	er	Gly	Tyr	Thr	Phe 150	Thr	Arg	Tyr	Thr	Met 155	His	Trp	Val	Lys	Gln 160
Arg P	ro	Gly	Gln	Gly 165	Leu	Glu	Trp	Ile	Gly 170	Tyr	Ilė	Asn	Pro	Ser 175	Arg
Gly T	_		180					185					190		
Thr A	_	195					200					205			
	210					215					220				•
Tyr C 225					230					235				-	240
Ser G				245					250					255	
Leu A			260			•		265					270		•
Gln S		275					280					285			
	290					295					300				
Val 8		_			310					315					320
Phe T				325					330					335	
His C			340					345					350		
Lys I		355					360					365			
	370					375					380				
Arg E 385					390					395					400
Phe S	ser	Ser	Tyr	Trp 405	Met	Asn	Trp	Val	Lys 410	Gln	Arg	Pro	GTÀ	Gln 415	GTÀ

Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr 420 425 430

Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser 435

Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala 450 455 460

Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr 465 470 475 480

Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser 485 490 495

Gly His His His His His 500